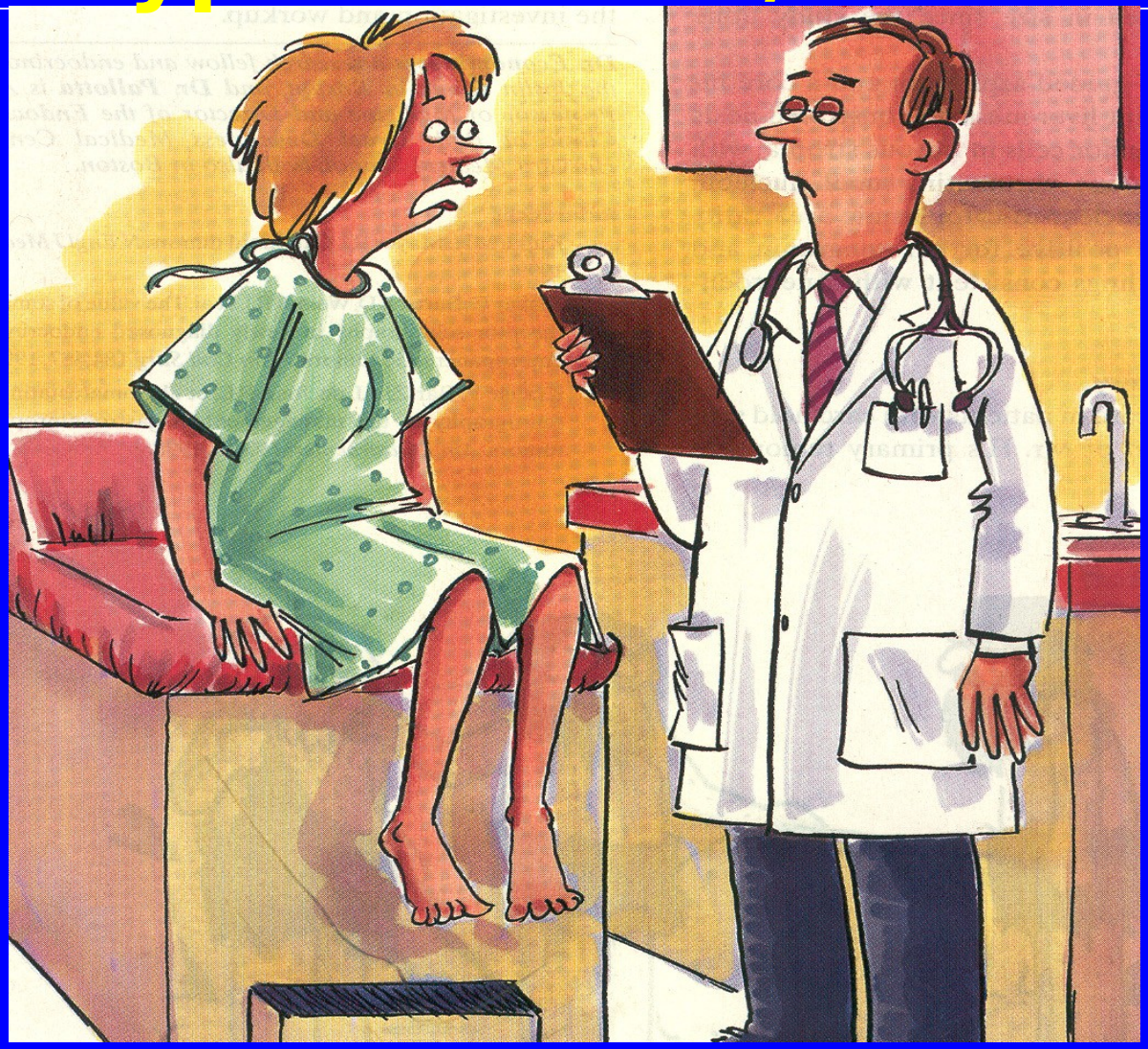
CHF Update 2004

Mark Cucuzzella MD FAAFP
Lt Col Colorado Air National Guard MC FS
Dept of Family Medicine
University of Colorado

“The art of Medicine consists of amusing the patients while nature cures the disease”
Voltaire

Unfortunately this does not work in Heart Failure

Not a Typical CHF F/U Visit



I feel great. Is that normal?

Objectives:

- Review epidemiology of CHF
- New ACC/AHA classification scheme
- Review common etiologies and diagnostic technique
- Discuss compensatory mechanisms in HF
- Old and new treatment modalities & evidence for their use

Introduction

- **5 million Americans with heart failure**
- **20% of hospital admissions in persons older than 65**
- **Prognosis for symptomatic heart failure worse than most cancers**
  - **1-yr mortality rate of 45%**
- **In people diagnosed with heart failure, sudden death occurs at 6 to 9 times the rate of the general population**
- ***2/3 treated by primary care MDs***
- **Radical changes in the treatment of heart failure in the past 10 yrs….but unfortunately**

Challenges-Why no meaningful reduction in mortality due to heart failure? (Framingham data)

- Diverse causes- not just poorly contracting ventricles
- Majority are elderly
- Victims of our own success- patients staying alive with other illness eventually dying of HF (i.e. MI, DM, HTN)
- Few women, racial minorities, and elderly have taken part in clinical trials
- Although heart failure is a major public health problem, there are *no national screening efforts*
- *Heart failure is largely preventable*, primarily through the control of blood pressure and other vascular risk factors

Pathogenesis of Heart Failure- I

IMPAIRED SYSTOLIC (CONTRACTILE) FUNCTION
Ischemic damage or dysfunction
- Myocardial infarction
- Persistent or intermittent myocardial ischemia
- Hypoperfusion (shock)

Chronic pressure overloading
- Hypertension
- Obstructive valvular disease

Chronic volume overload
- Regurgitant valvular disease
- Intracardiac left-to-right shunting
- Extracardiac shunting

Nonischemic dilated cardiomyopathy
- Familial/genetic disorders
- Toxic/drug-induced damage
- Immunologically mediated necrosis
- Infectious agents
- Metabolic disorders
- Infiltrative processes
- Idiopathic conditions

DIASTOLIC FUNCTION (RESTRICTED FILLING, INCREASED STIFFNESS)
Pathologic myocardial hypertrophy
- Primary (hypertrophic cardiomyopathies)
- Secondary (hypertension)

Aging
Ischemic fibrosis
Restrictive cardiomyopathy
- Infiltrative disorders (amyloidosis, sarcoidosis)
- Storage diseases (hemochromatosis, genetic abnormalities)

Endomyocardial disorders

Cecil's 2004

Pathogenesis of Heart Failure-II

MECHANICAL ABNORMALITIES
Intracardiac
- Obstructive valvular disease
- Regurgitant valvular disease
- Intracardiac shunts
- Other congenital abnormalities

Extracardiac
- Obstructive (coarctation, supravalvular aortic stenosis)
- Left-to-right shunting (patent ductus)

DISORDERS OF RATE AND RHYTHM
Bradyarrhythmias (sinus node dysfunction, conduction abnormalities)
Tachyarrhythmias (ineffective rhythms, chronic tachycardia)

PULMONARY HEART DISEASE
Cor pulmonale
Pulmonary vascular disorders

HIGH-OUTPUT STATES
Metabolic disorders
- Thyrotoxicosis
- Nutritional disorders (beriberi)

Excessive blood flow requirements
- Chronic anemia
- Systemic arteriovenous shunting

Cecil's 2004

Definitions of Heart Failure

- **“Heart failure may be considered to be the condition in which an abnormality of cardiac function is responsible for the inability of the heart to pump blood at a rate commensurate with the requirements of the metabolizing tissues…” E. Braunwald**

- **“Heart failure represents a syndrome in which cardiac dysfunction is associated with reduced exercise tolerance, a high incidence of ventricular arrhythmias, and shortened life expectancy.” J.N. Cohn**

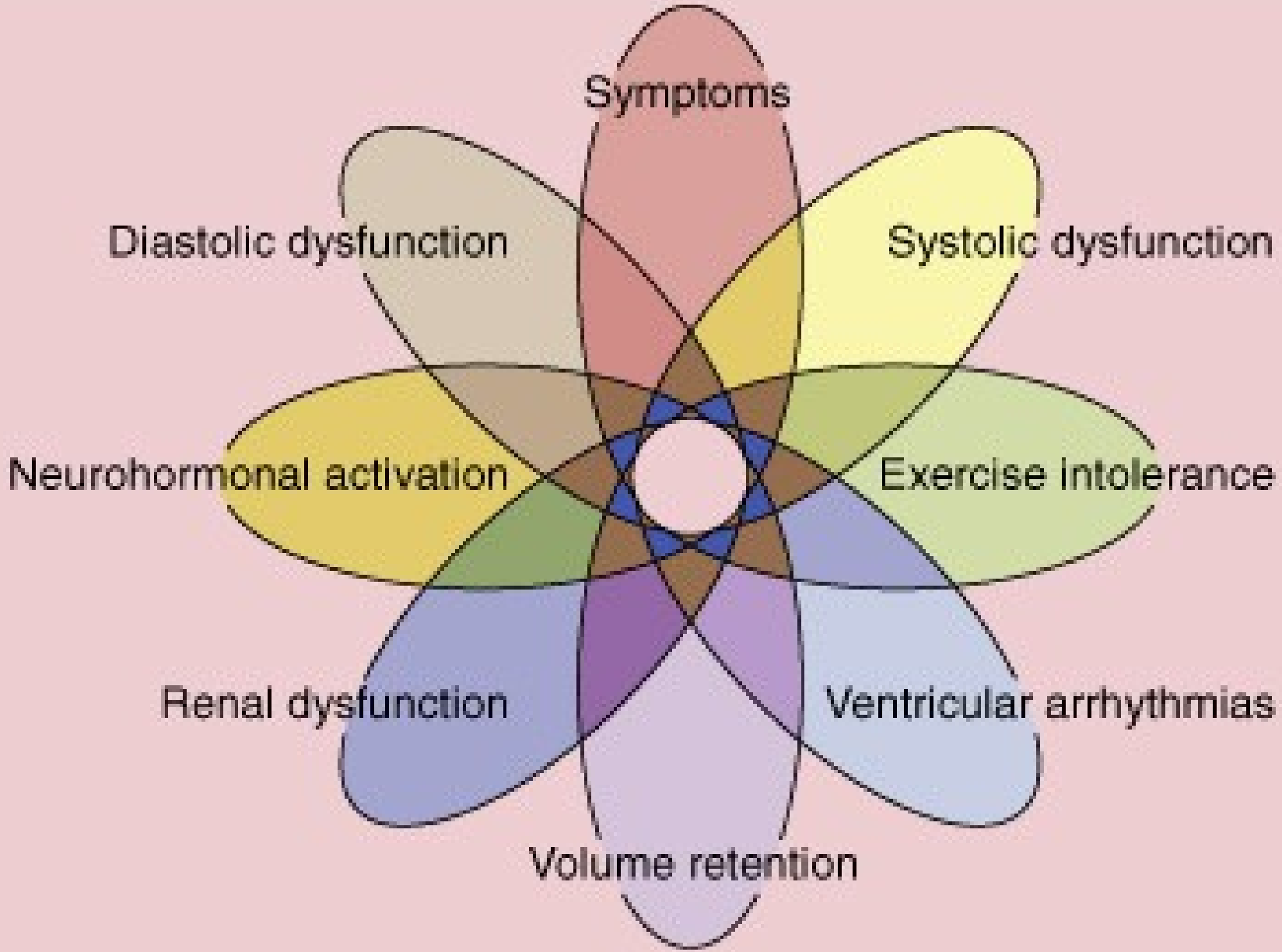
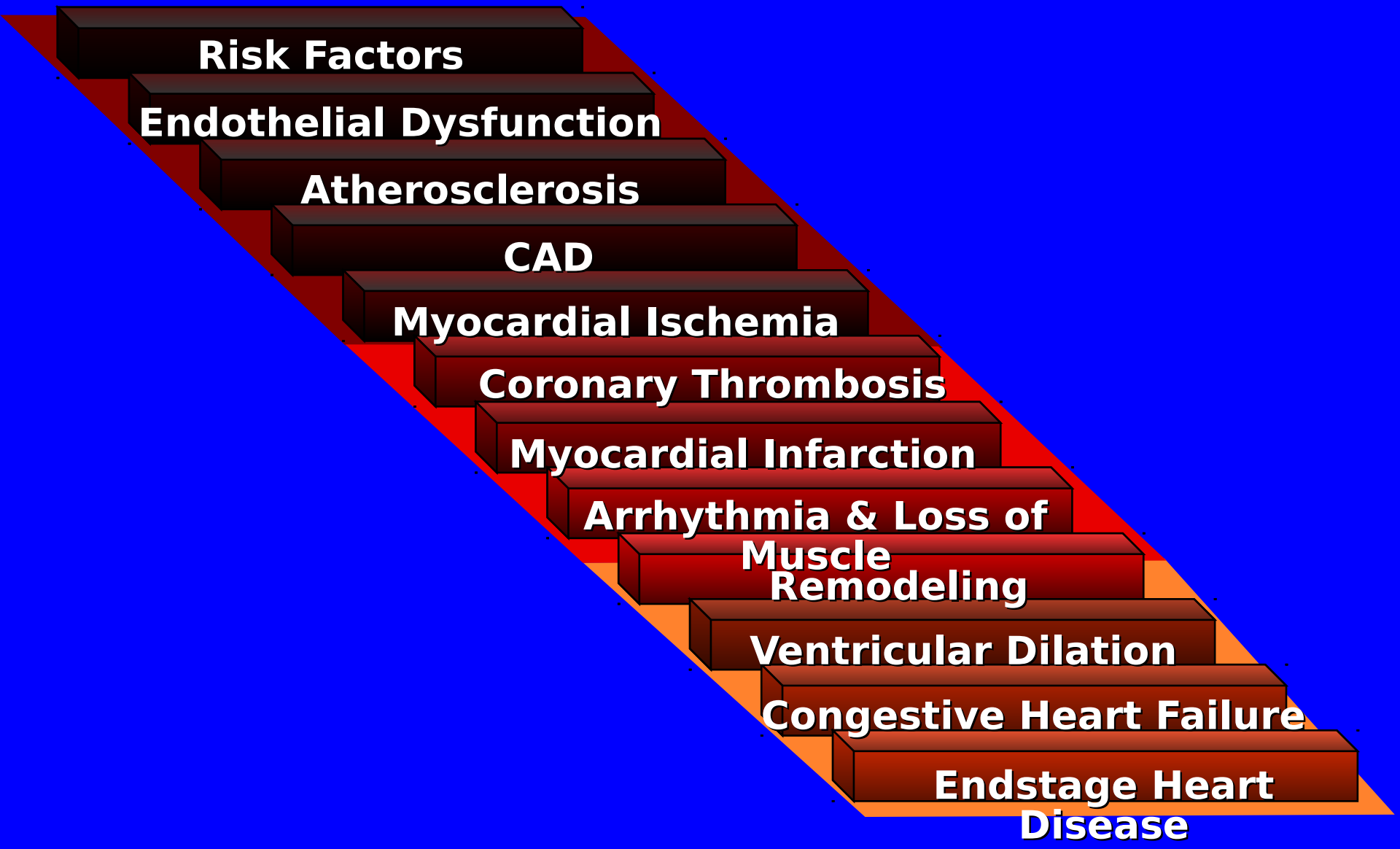


Table 1. New York Heart Association Class and Prognosis*

Class	Definition	Prognosis†
I	No limitation of physical activity	20% Mortality at 5 years[2]
II	Slight limitation of physical activity and symptoms with ordinary activity (eg, climbing stairs)‡	3% to 25% Mortality per year[3]
III	Marked limitation of physical activity and symptoms with less than ordinary activity (eg, bathing, walking across room)‡	10% to 45% Mortality per year[3]
IV	Inability to carry on any physical activity without discomfort and symptoms at rest‡	40% to 50% Mortality at 1 year[4]

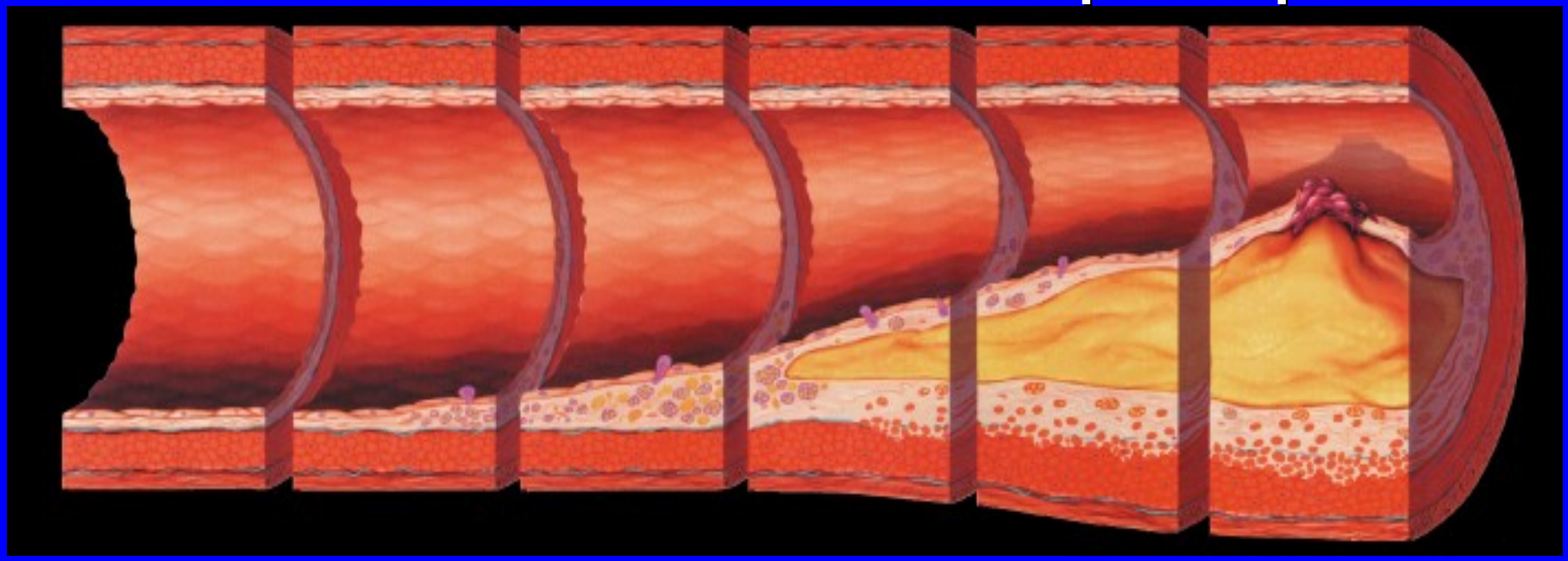
Problem- Very Subjective

The Progressive Development of Cardiovascular Disease



Atherosclerosis Timeline

Foam Cells
Fatty Streak
Intermediate Lesion
Atheroma
Fibrous Plaque
Complicated Lesion/ Rupture



Endothelial Dysfunction

From First Decade

From Third Decade

From Fourth Decade

Adapted from Pepine CJ. *Am J Cardiol.* 1998;82(suppl 104).

New HF Classification: Evolution and Disease Progression

- **Four Stages of HF (ACC/AHA Guidelines):**
  - **Stage A: high risk for developing HF with no structural disorder of the heart**
  - **Stage B: structural disorder without symptoms of HF**
  - **Stage C: past or current symptoms of HF associated with underlying structural heart disease**
  - **Stage D: end-stage disease who requires specialized treatment strategies**

Hunt, SA, et al ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult, 2001

New ACC/AHA Classification

- Recognizes established risk factors and structural abnormalities
- Progressive nature
- Cannot go back from D to C…
- NYHA based on symptoms- can reverse
- Underscores the importance of treatment strategies *as well as preventative efforts*

Probably Stage B

Should he get a new running mate?

Defining the problem

- **Systolic dysfunction: Difficulty emptying the left ventricle.**
  - **Reduced ejection fraction (< 40%)**
- **Diastolic dysfunction: Inability to fill and relax the left ventricle.**
  - **Elevated end diastolic pressure**
  - **Normal sized chamber**
- **Most patients have component of both**
- **May define with *preserved* or *impaired* LV function**

Impaired Left Ventricular Systolic Function (EF<40%)

- Injury and/or stress to myocardium
- Progressive process- Cardiac Remodeling
  - Chamber dilates
  - Hypertrophies
  - Becomes more spherical
- Process sustained and exacerbated without intervention

Diastolic Heart Failure

- 20-50% of heart failure patients have preserved LV function
- Cardiac output is limited by abnormal filling (particularly during exercise)
- Elevated LVEDP→pulmonary congestion→dyspnea and edema
- Equal rates of hospitalization and, possibly, mortality
- No RCTs- *Clinical Evidence 2004*

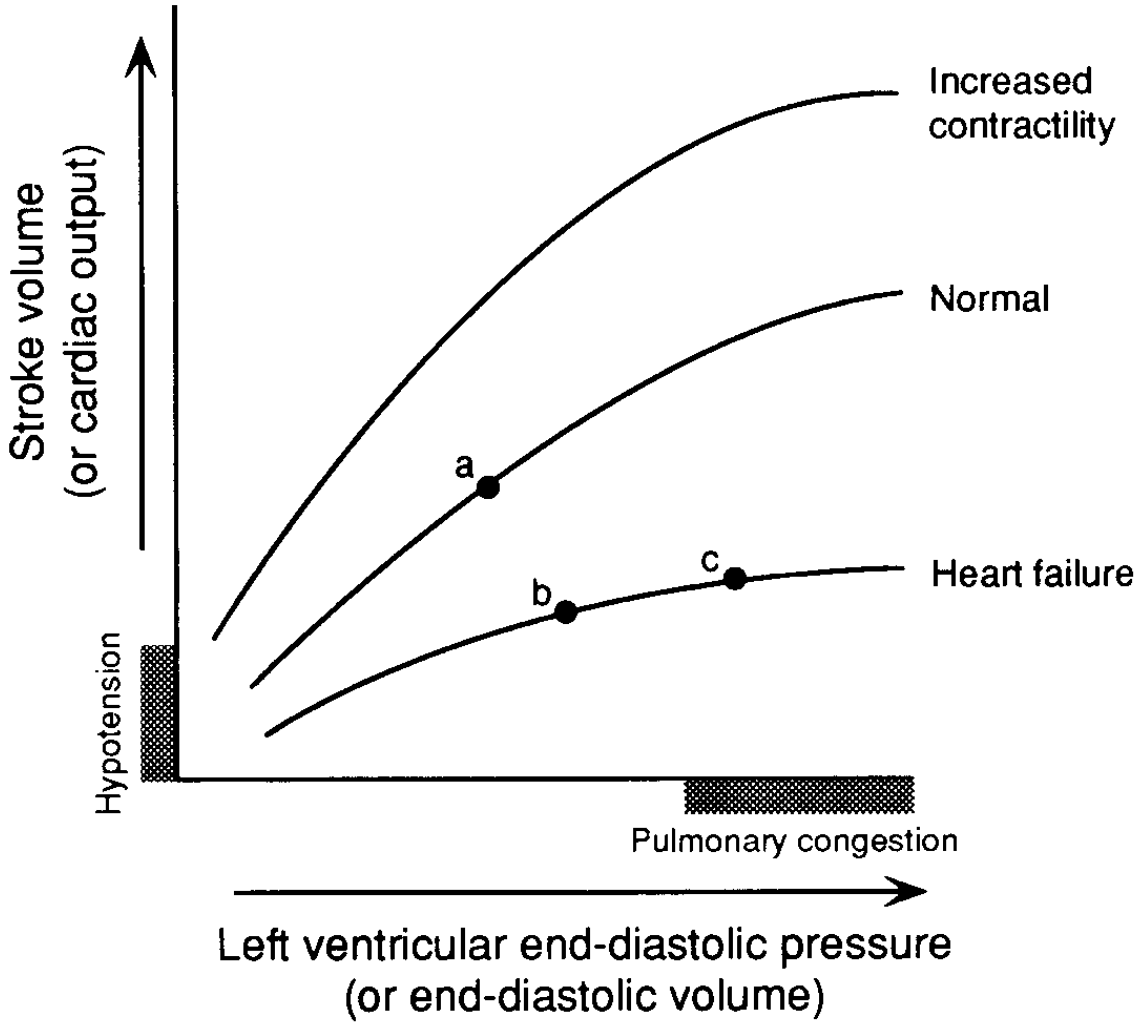
Compensatory Mechanisms

- Frank-Starling Mechanism
- Neurohormonal Activation
- Ventricular Remodeling

The Old Theory

- Purely Hemodynamic model
- Altered load on the failing ventricle
- Treatment strategies involved improving the hemodynamics
  - Vasodilators, diuretics, and inotropic agents

Frank-Starling Mechanism



a. At rest, no HF

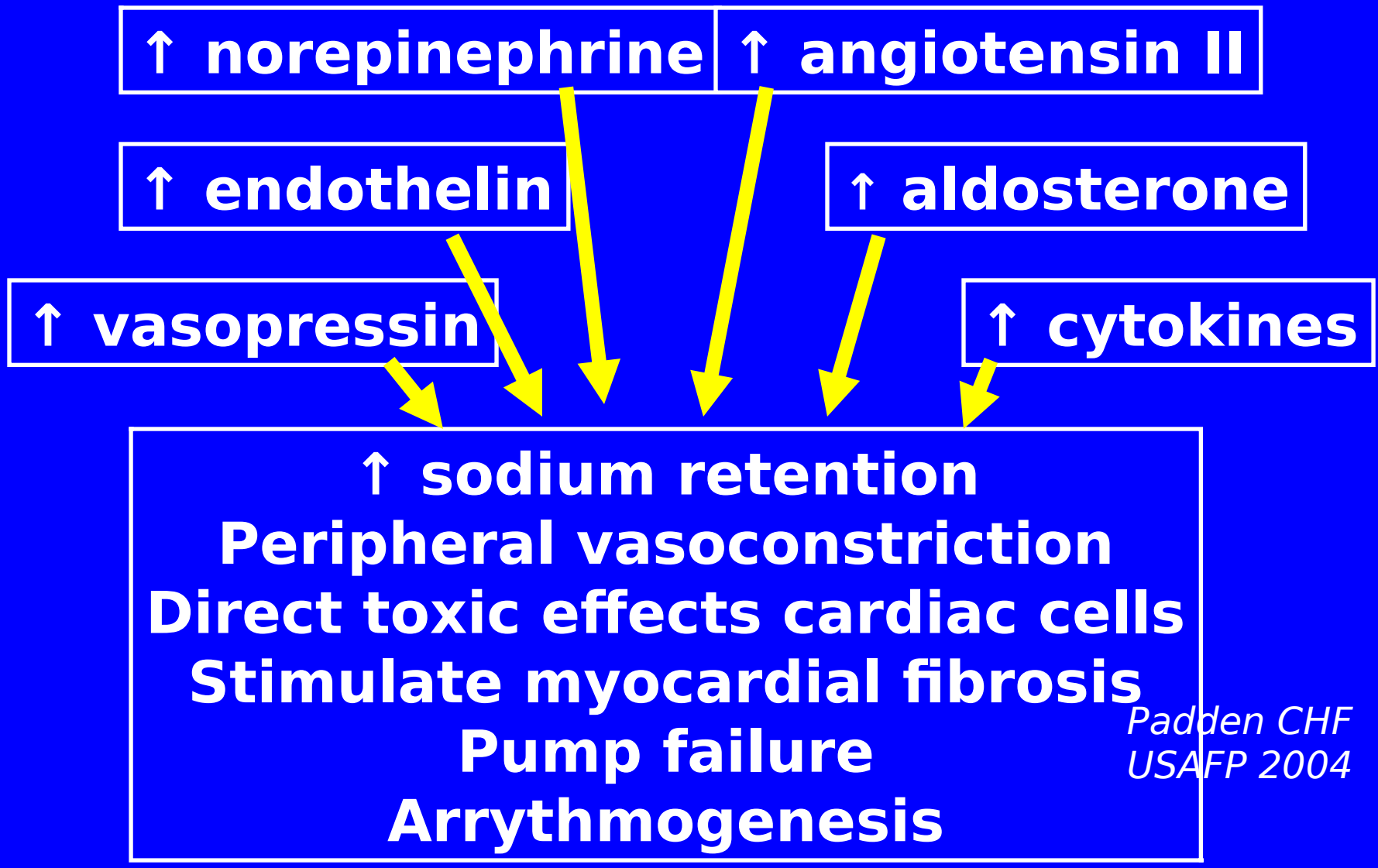
b. HF due to LV systolic dysfunction

c. Advanced HF

Neurohormonal Activation

- Not just a cardiac disease!
- ↓ LV Function ↓ Cardiac output activate:
  - Sympathetic nervous system (SNS)
  - Renin-angiotensin-aldosterone system (RAAS)
  - Vasopressin (a.k.a. antidiuretic hormone, ADH)
- Counteregulatory systems
  - ANP, Bradykinin, Nitrous Oxide
- Balance in these systems may determine disease severity

Pathophysiology of CHF



Padden CHF
USAFP 2004

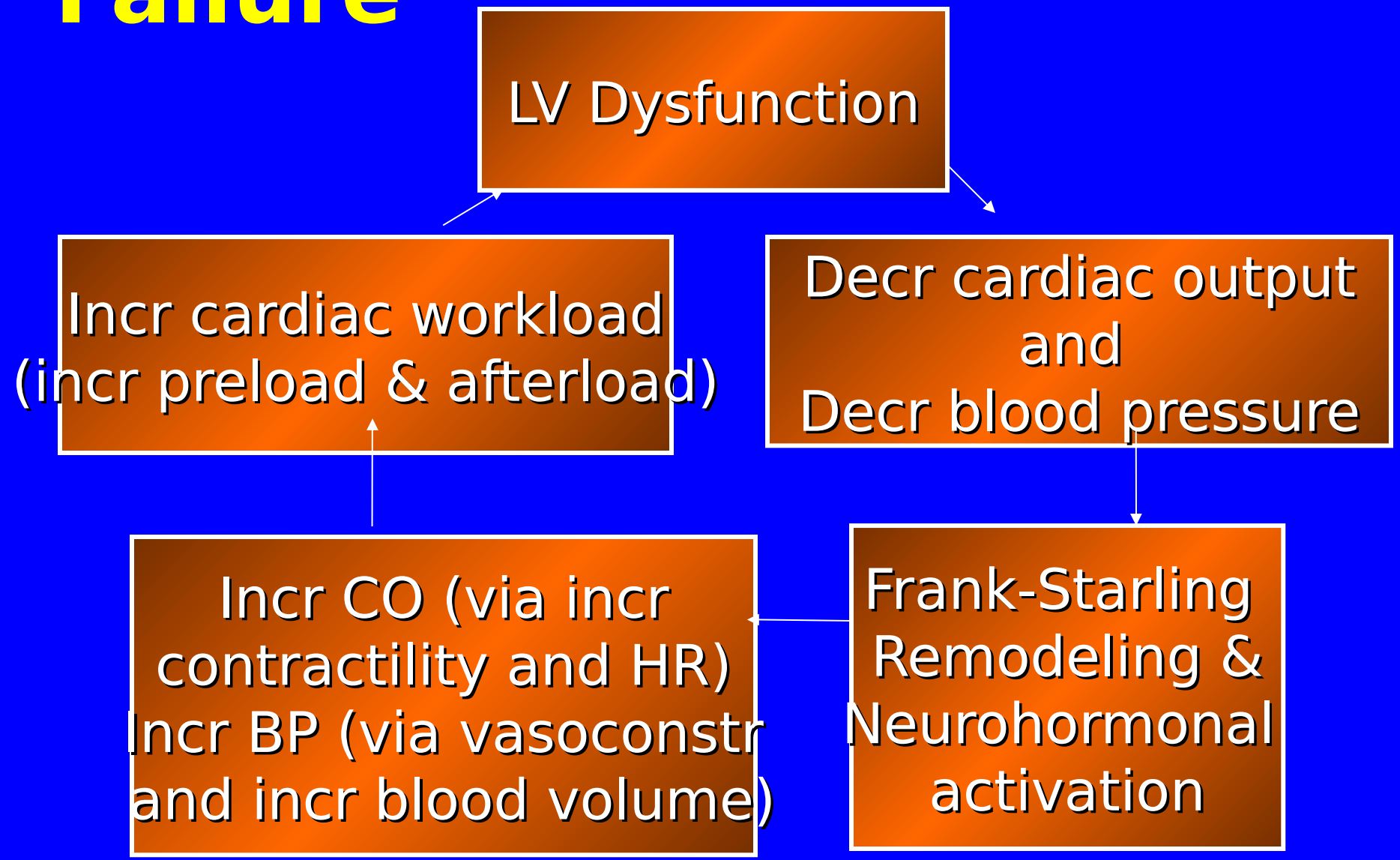
Neurohormonal Responses to Impaired Cardiac Performance

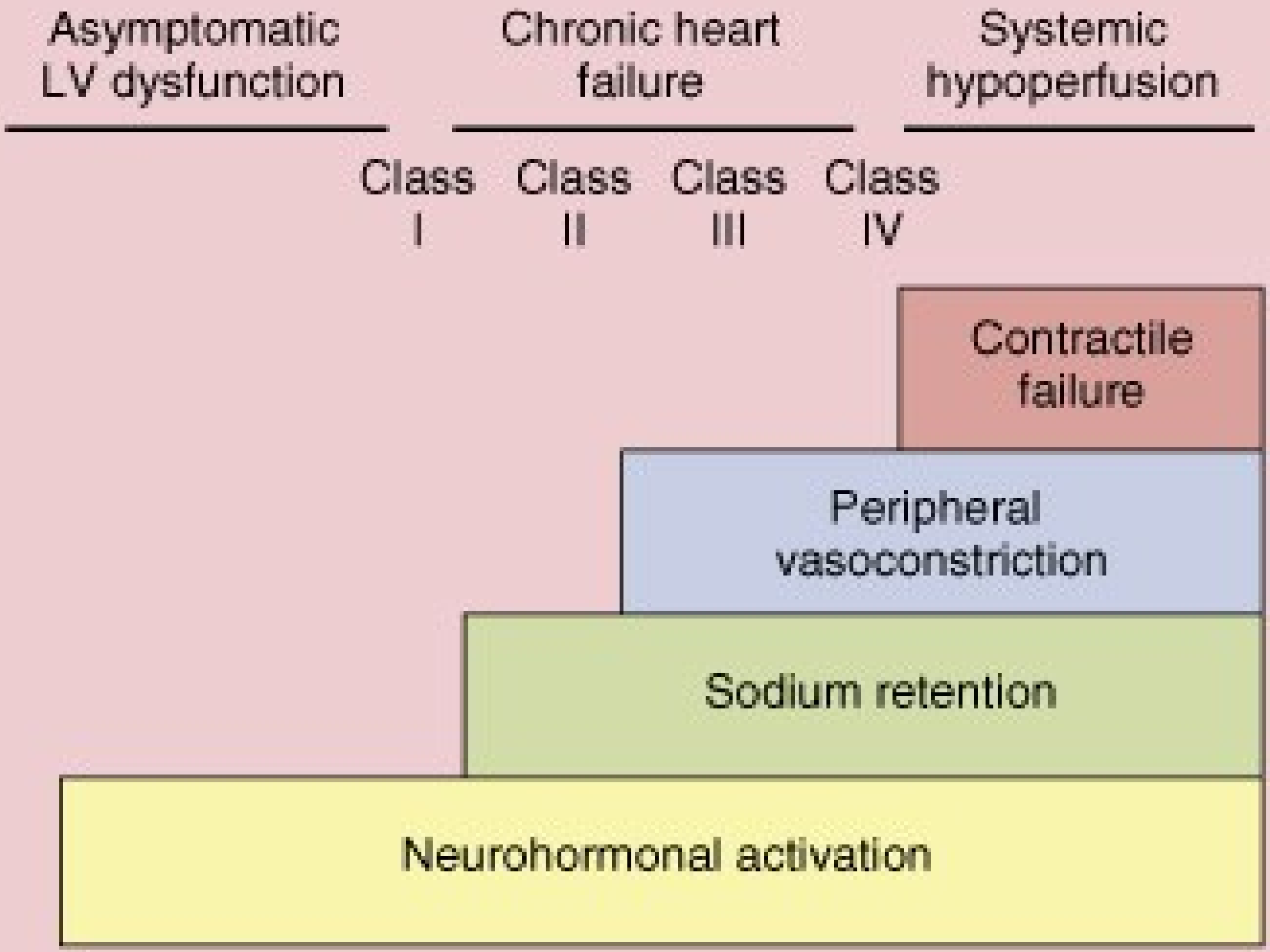
Initially Adaptive, Deleterious if Sustained

Response	Short-Term Effects	Long-Term Effects
Salt and Water Retention	Augments Preload	Pulmonary Congestion, Anasarca
Vasoconstriction	Maintains BP for perfusion of vital organs	Exacerbates pump dysfunction (excessive afterload), increases cardiac energy expenditure
Sympathetic Stimulation	Increases HR and ejection	Increases energy expenditure

Jaski, B, MD: Basics of Heart Failure: A Problem Solving Approach

Vicious Cycle of Heart Failure

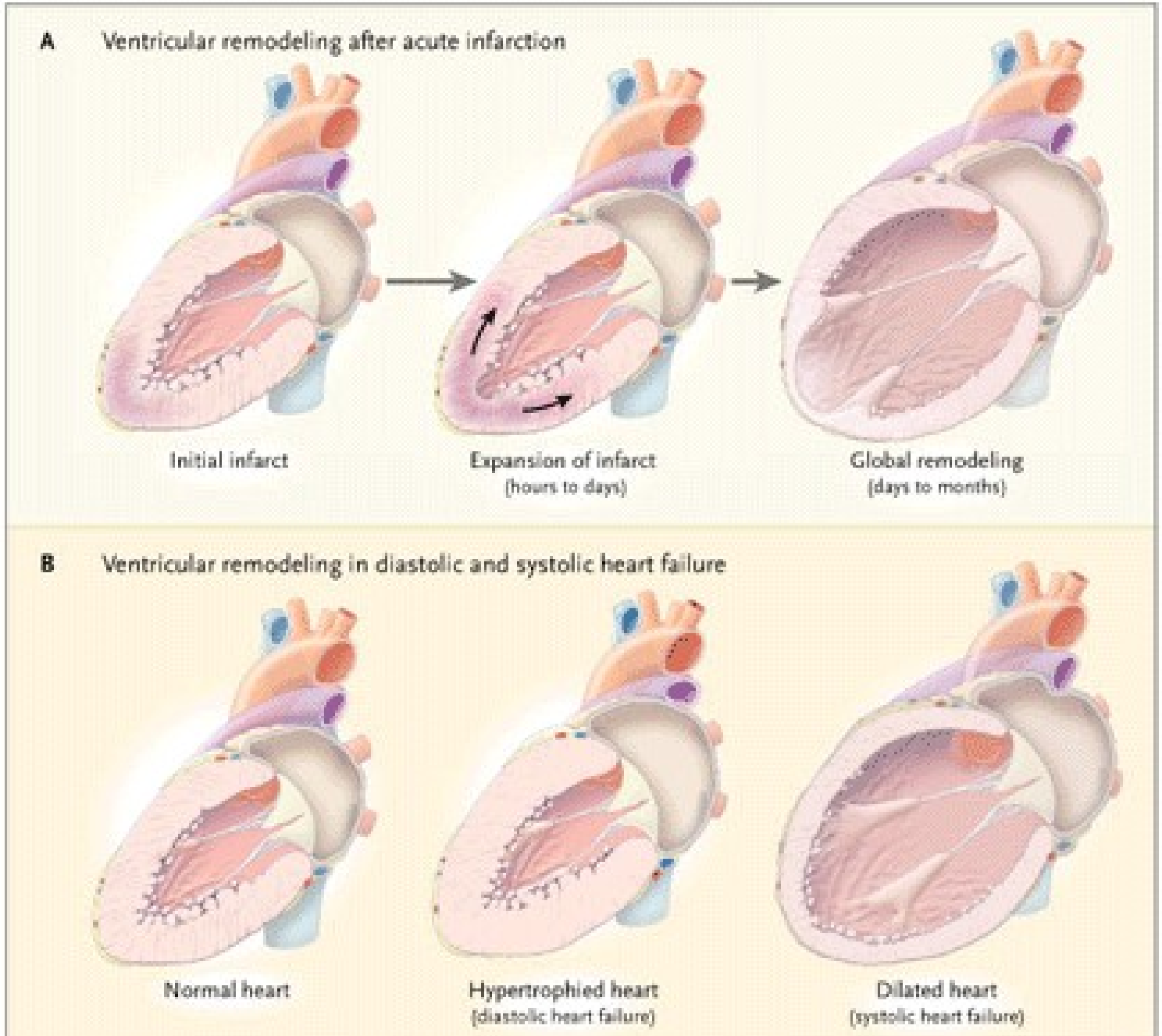




Remodeling

Remodeling

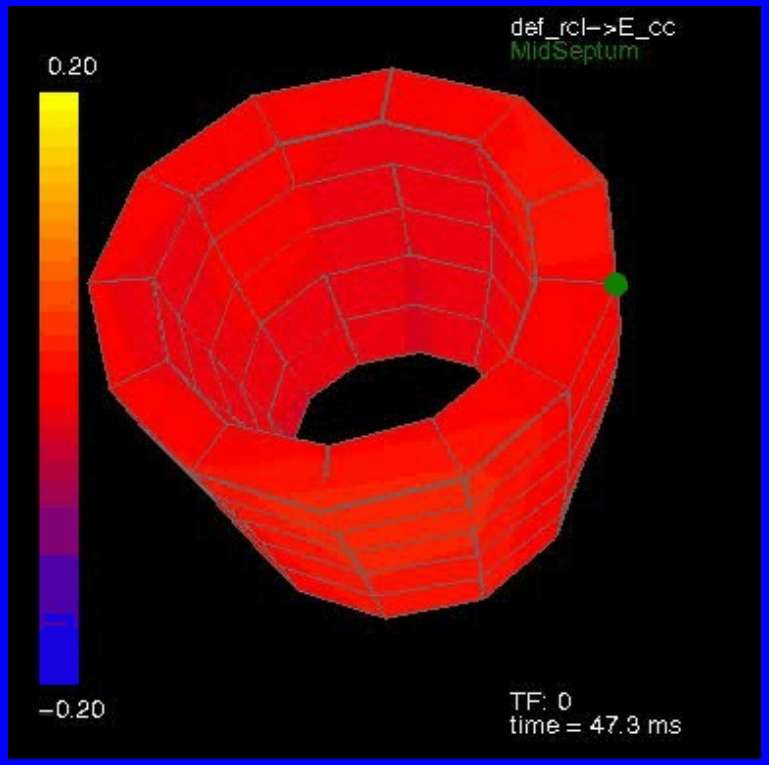
- LV affected by mechanical and neurohormonal factors
- Occurs in MI, cardiomyopathy, HTN, and valvular heart disease
- Hypertrophy
- Loss of myocytes- apoptosis and necrosis
- Fibrosis
- Therapies have been directed at increasing “reverse remodeling”
  - B-blkers, ACE- inhibitors, cardiac resyncronization

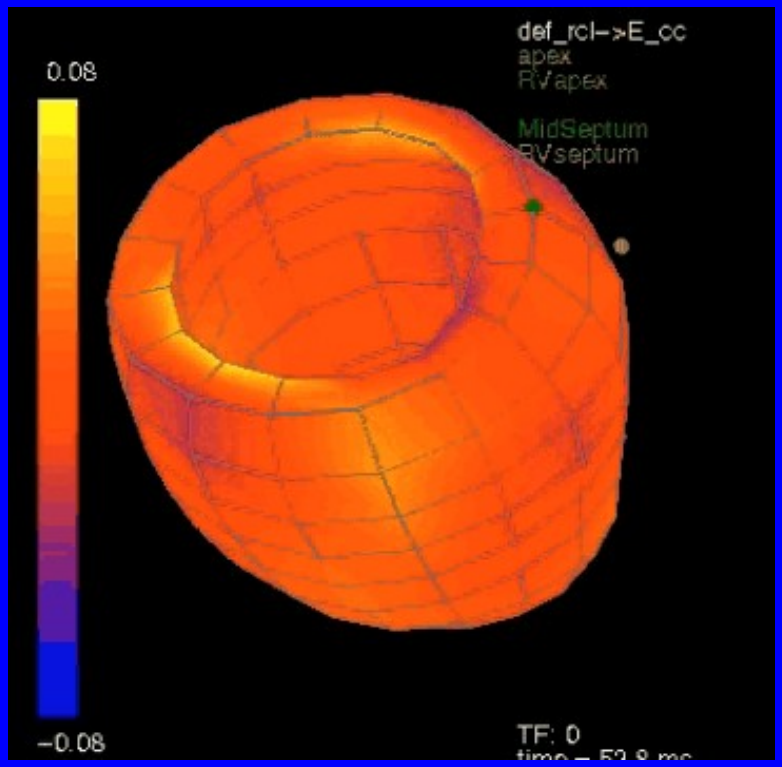


Jessup and Brozena. Heart Failure; NEJM. 348:2007-18, May 03

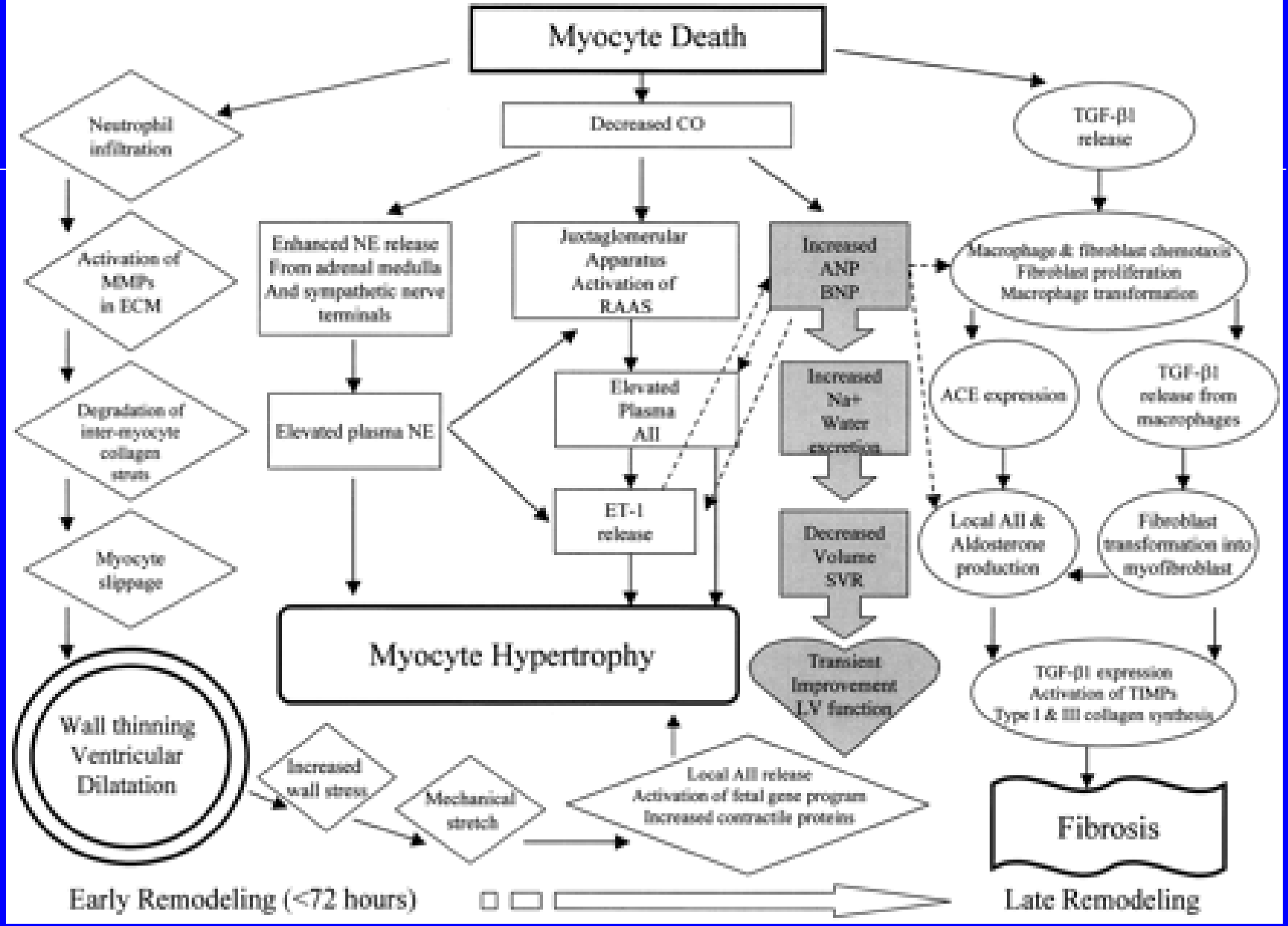
Compensatory Mechanisms- Ventricular Remodeling

Alterations in the heart's size, shape, structure, and function brought about by the chronic hemodynamic stresses experienced by the failing heart.





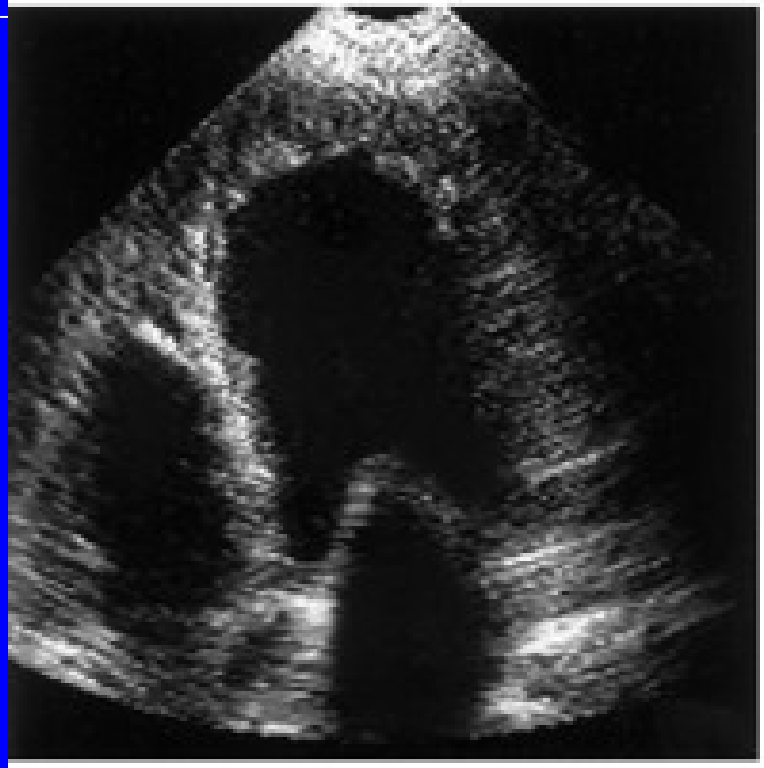
Curry CW, et al Circulation 2000 Jan 4;101(1):E2.



Circulation. 2000 Jun 27;101(25):2981-8.
Left ventricular remodeling after myocardial infarction:pathophysiology and therapy

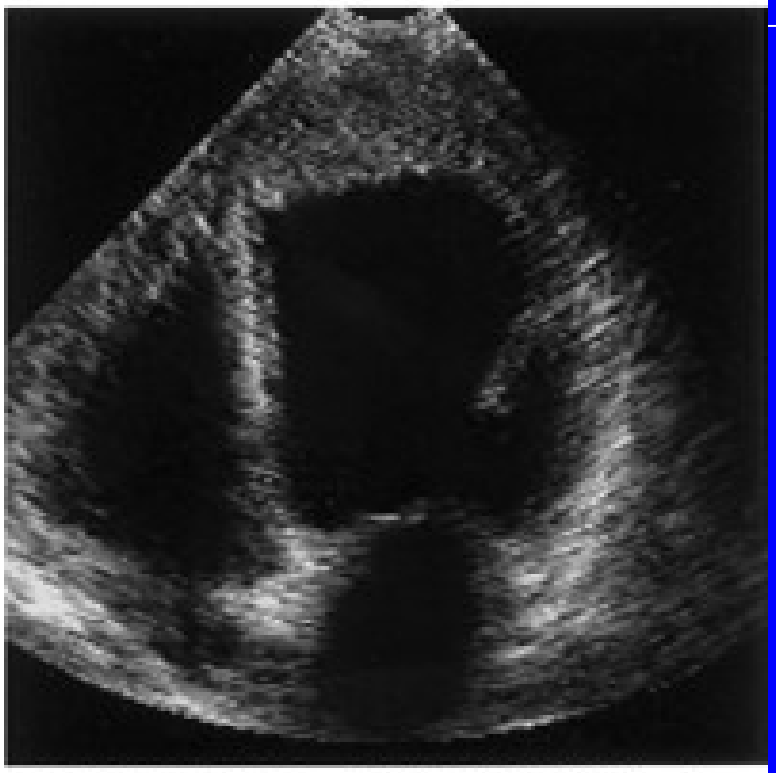
LV Remodeling Post Anteroseptal MI

1 week



EDV 137ml ESV 80ml
EF 41%

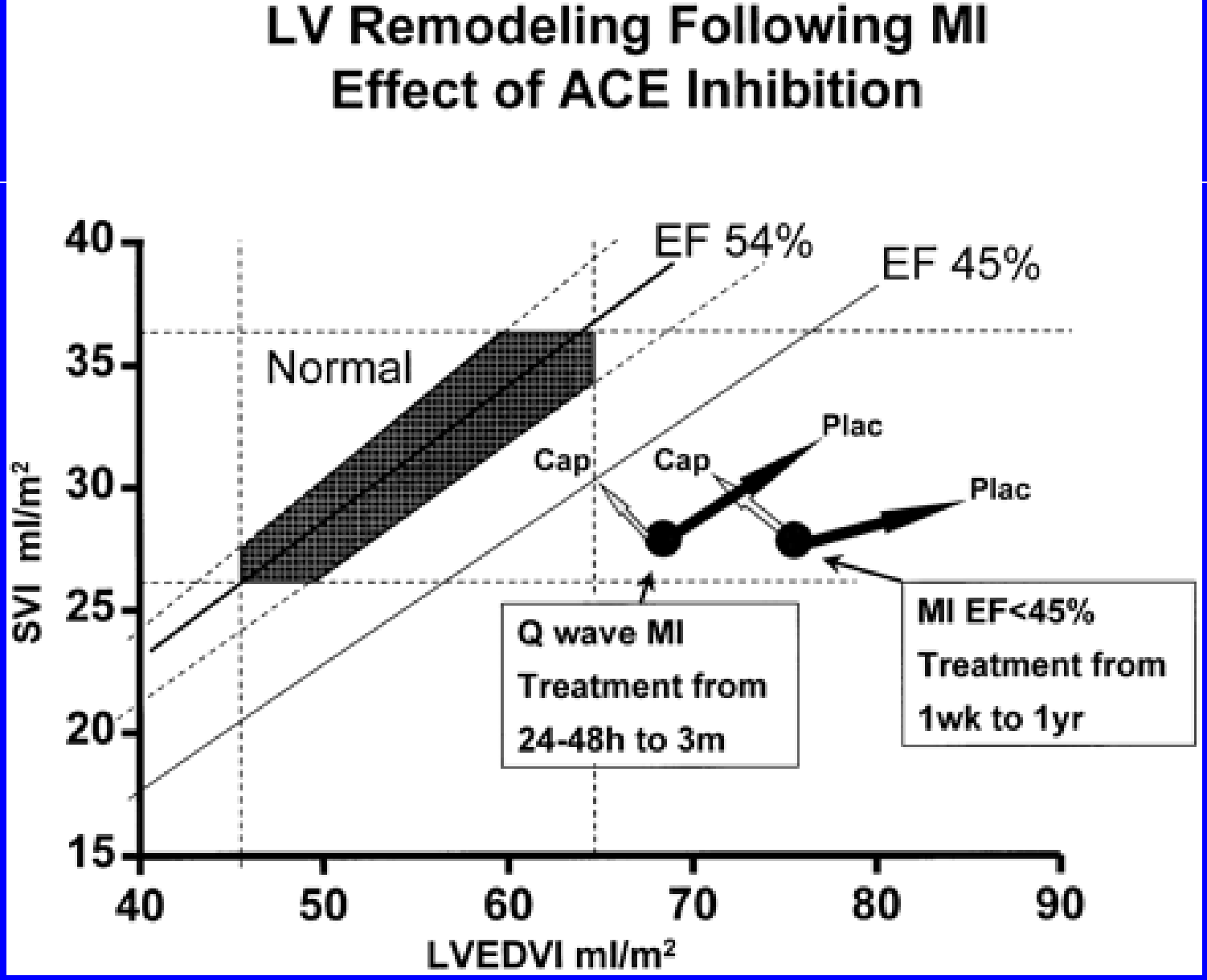
3 months



EDV 189ml ESV 146ml
EF 23%

Apical 4 Chamber View
End-diastole

Circulation. 2000 Jun 27;101(25):2981-8.
Left ventricular remodeling after myocardial infarction: pathophysiology and therapy



Circulation. 2000 Jun 27;101(25):2981-8.
Left ventricular remodeling after myocardial infarction:pathophysiology and therapy

Arrhythmias and BB blocks

- Remodeling also effects the conduction system
- Elevated LVEDP leads to atrial stretch
  - Supraventricular arrhythmias
- Abnormal myocyte conduction leads to LBBB
  - Significant predictor of sudden death (6-9 X general population)
  - Abnormal ventricular activation and contraction, dysyncrony, valve functioning, and diastolic function
  - Reduced EF, arterial pressure, increase LV volume, and MR
  - Ventricular arrhythmias 2ary to dispersion of normal conduction through non homogenous myocardial tissue

Assessing Heart Failure

- Patient History
  - Symptom, Serial weights
- Physical Examination
  - JVD, HJR, gallop rhythm, edema, perfusion
- Laboratory and Diagnostic Tests
  - BNP, Lytes, Echo, EKG

Left Ventricular Dysfunction Systolic and Diastolic

- **Symptoms**
  - **Fatigue**
  - **SOB on exertion, at rest in advanced cases**
  - **Orthopnea**
  - **PND**
  - **Nocturia**
  - **Mental status changes**
  - **+/- Anorexia**
  - **+/- Abdominal Pain**
- **Physical Signs**
  - **Basilar Rales**
  - **Pulmonary Edema**
  - **S3 Gallop**
  - **Pleural Effusion**

Right Ventricular Failure Systolic and Diastolic

- Symptoms
  - Abdominal Pain
  - Anorexia
  - Nausea
  - Bloating
  - Swelling
- Physical Signs
  - Peripheral Edema
  - Jugular Venous Distention
  - Abdominal-Jugular Reflux
  - Hepatomegaly

Diagnostic Evaluation of New Onset Heart Failure

- Determine the type of cardiac dysfunction (systolic vs. diastolic)
- Determine Etiology
- Define prognosis
- Guide therapy

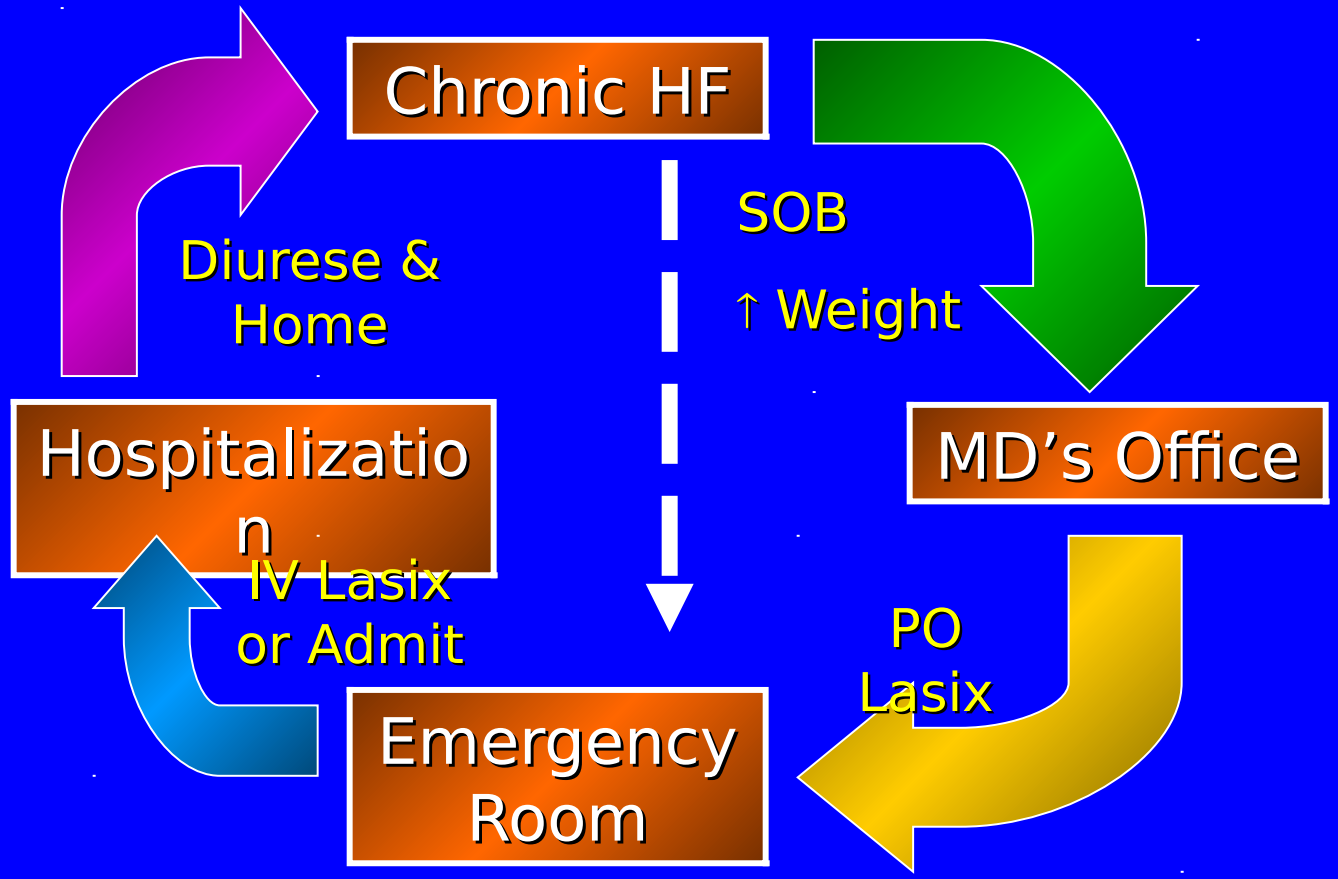
B-Type Natriuretic Peptide

- Cardiac neurohormone secreted by the ventricles in response to volume expansion and pressure overload
- Has a natriuretic and vasodilatory effect
- Suppresses the renin-angiotensin-aldosterone system
- Clearance rapid- ½ life 20 minutes
- Rises with age
- >100 abnormal… but pts with CHF are baseline high
- Marker of ventricular filling pressures

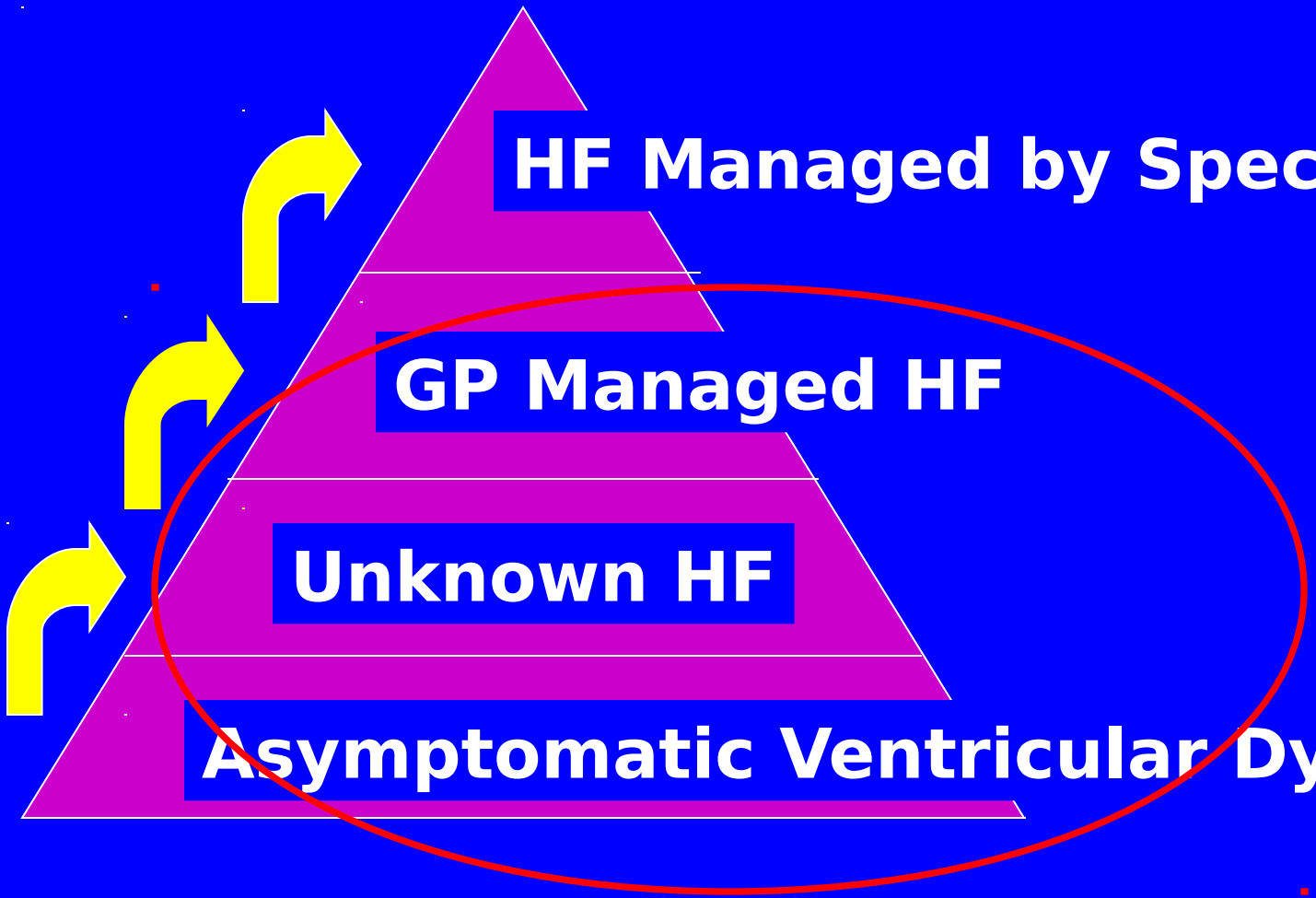
BNP Many Uses

- Diagnosis
  - 3 large studies - patients with symptoms of heart failure- BNP over 80 is between 92-98% sensitive
  - However, studies showed that pt's w/ LV dysfunction, but no heart failure symptoms also had elevated BNP levels, making it somewhat non-specific
- Prognosis
  - patients discharged from the hospital with elevated BNP levels have a worse prognosis
  - Pt's w/ higher BNP levels also had worsening of their functional class in the ensuing year
- Guide Therapy

THERAPY- The Vicious Cycle of Heart Failure Management



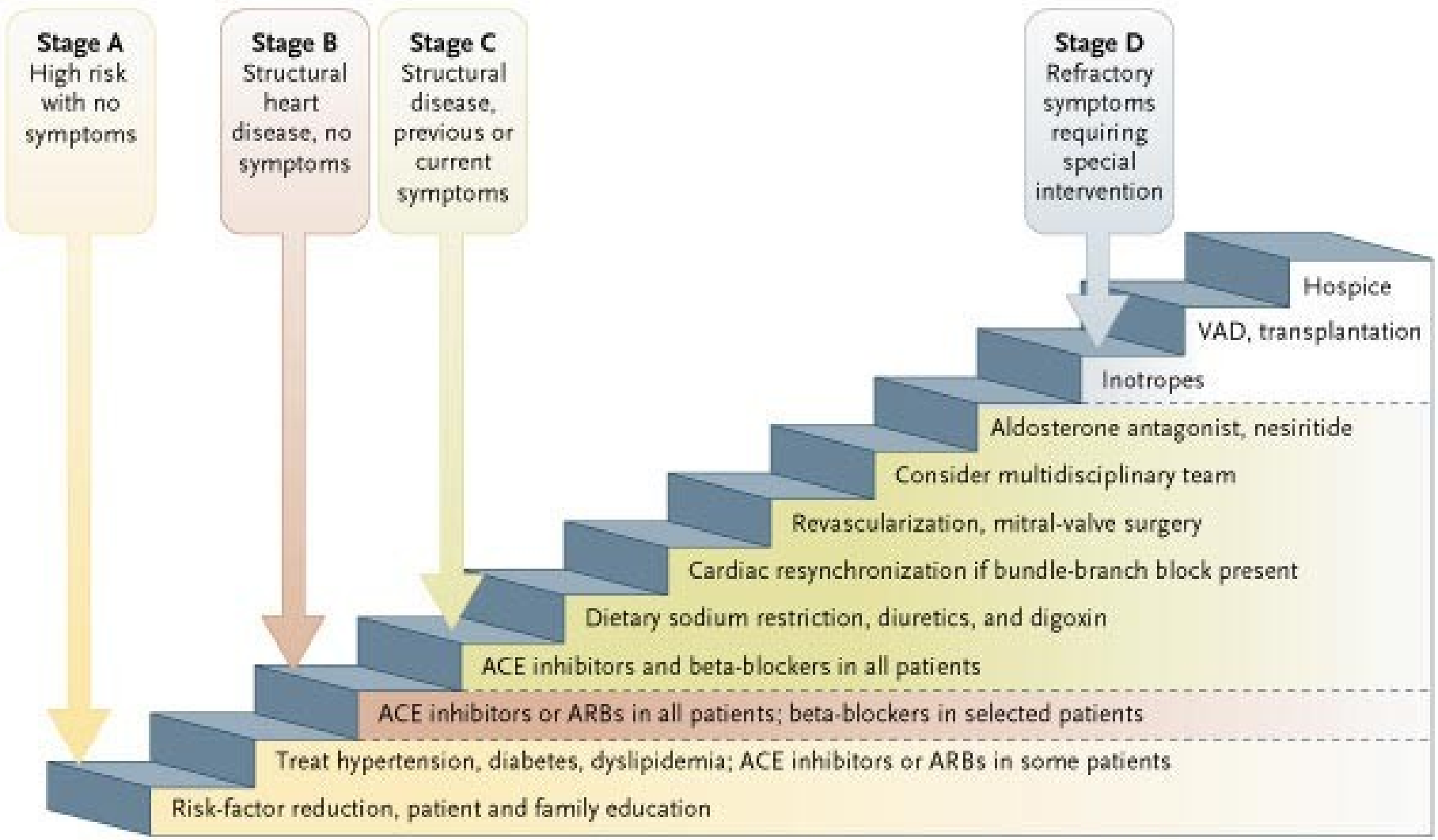
Natural History of CHF



Padden CHF USAFP 2004

Jessup and Brozena. Heart Failure; NEJM. 348:2007-18, May 03

Treatment Overview



General Measures

Lifestyle Modifications:

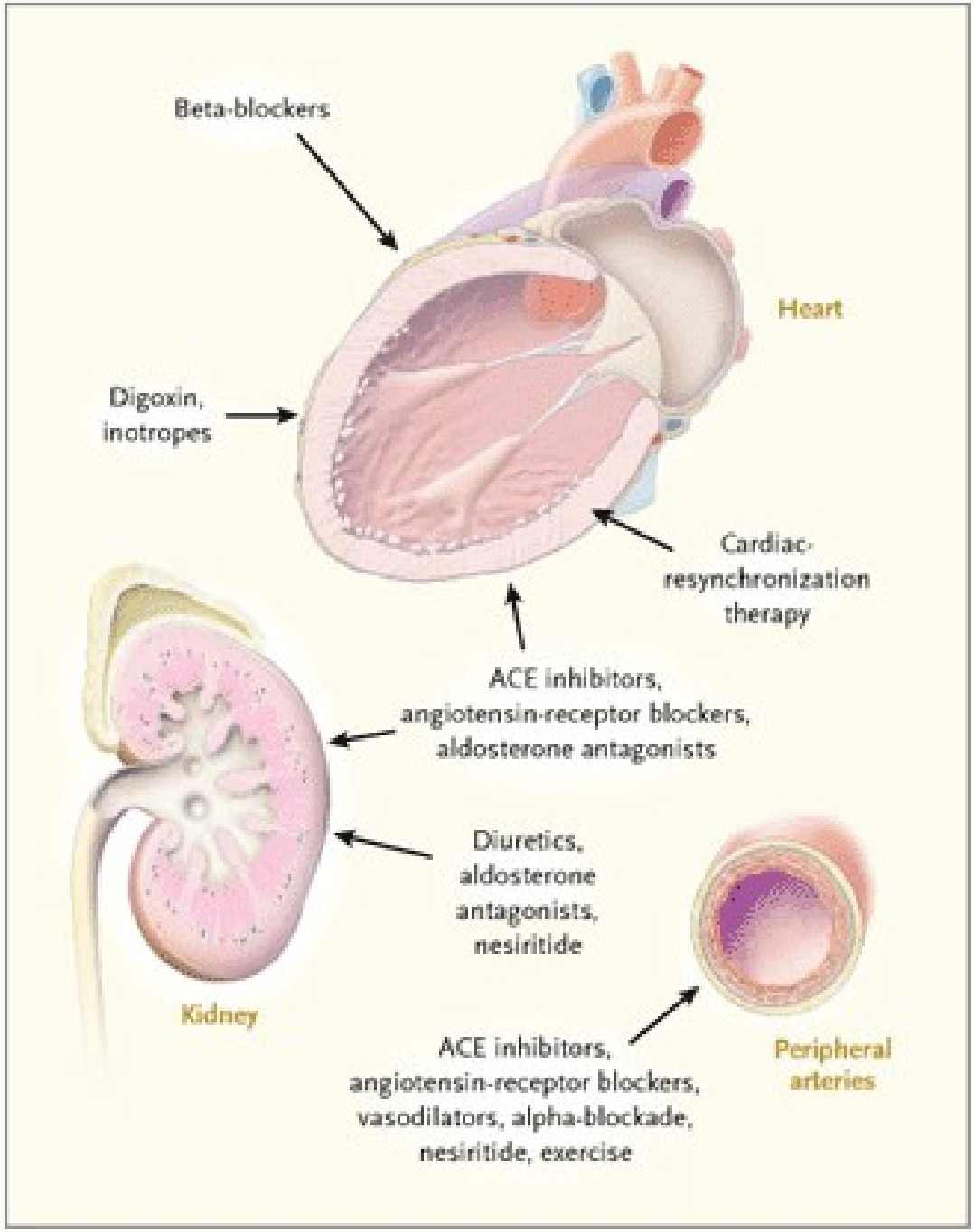
- Weight reduction
- Discontinue smoking
- Avoid alcohol and other cardiotoxic substances
- Exercise

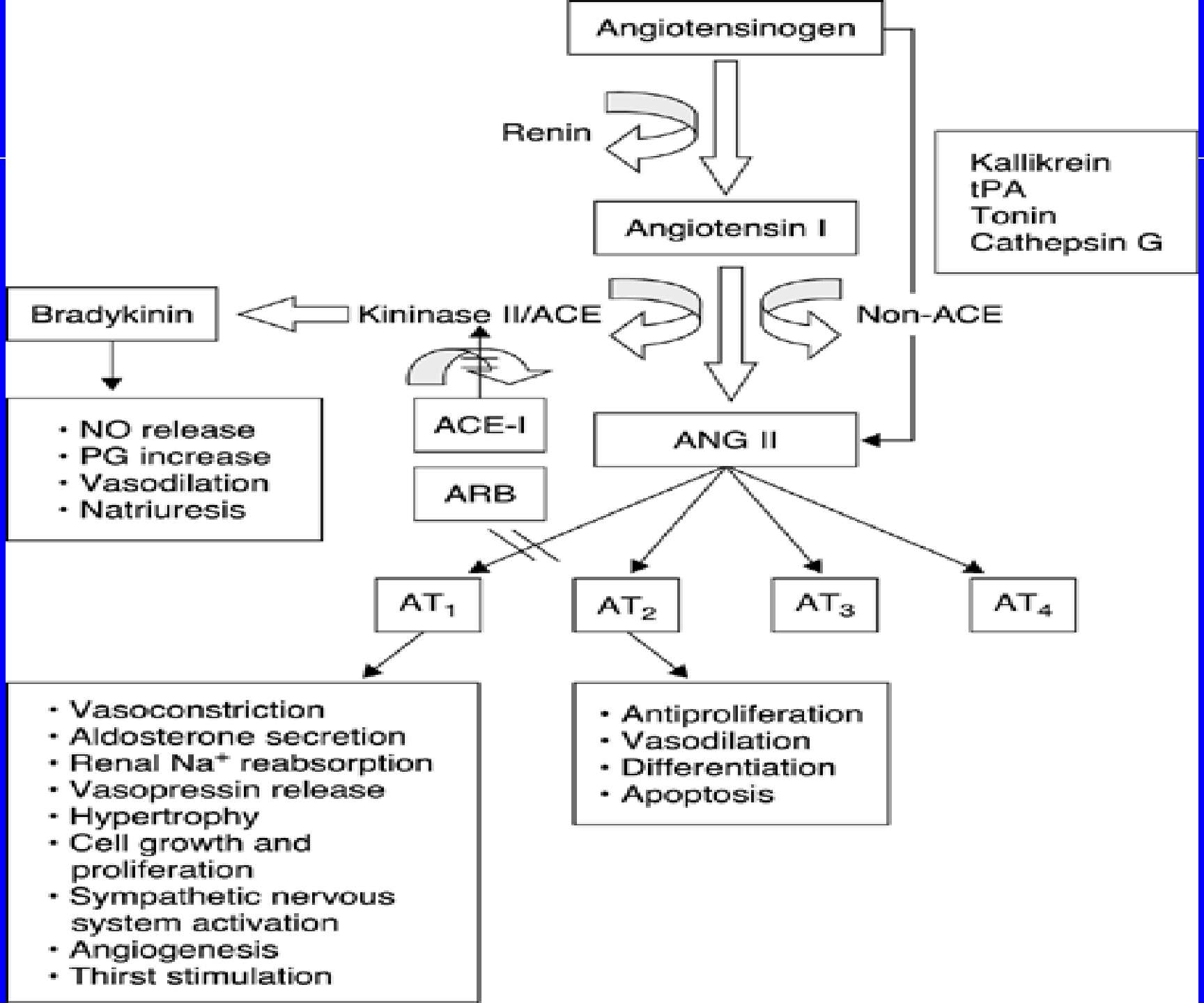
Medical Considerations:

- Treat HTN, hyperlipidemia, diabetes, arrhythmias
- Coronary revascularization
- Anticoagulation
- Immunization
- Sodium restriction
- Daily weights
- Close outpatient monitoring

- Medical approach
- Targeting several organ systems

Jessup and Brozena. Heart Failure; NEJM. 348:2007-18, May 03




Angiotensinogen
Renin
Angiotensin I
Kallikrein
tPA
Tonin
Cathepsin G
Bradykinin
Kininase II/ACE
Non-ACE
• NO release
• PG increase
• Vasodilation
• Natriuresis
ACE-I
ARB
ANG II
AT1
AT2
AT3
AT4
• Vasoconstriction
• Aldosterone secretion
• Renal Na+ reabsorption
• Vasopressin release
• Hypertrophy
• Cell growth and proliferation
• Sympathetic nervous system activation
• Angiogenesis
• Thirst stimulation
• Antiproliferation
• Vasodilation
• Differentiation
• Apoptosis

ACE Inhibitors

- Recommended for all heart failure patients
- Relieves symptoms and improves exercise tolerance
- Reduces risk of death and decreases disease progression
- Trials- CONCENSUS, V- HeFT II, SAVE, SOLVD
- Pooled data- decrease mortality 23% comp to placebo or vasodilator tx
- Benefits may not be apparent for 1-2 months after initiation

ACE Inhibitors – Proper Dosing

- ATLAS
  - High (32-35) vs low (2.5 – 5) dose Lisinopril
  - No change in mortality but decr hospitalizations in high dose group
- NETWORK
  - High (10 BID) vs Low (2.5 BID) Enalapril
  - Less mortality but higher combo of death + hosp with high dose
- Begin low and titrate to maximum tolerated for BP control
- Check RF and K+ 1-2 weeks after initiation and q 2-3 mos thereafter
- Creatinine expected to ↑ with ACE-I and Diuretic
- Lower dose to allow B-Blocker

Angiotensin Receptor Blockers (ARBs)

- Block AT_1 receptors, which bind circulating angiotensin II
- Examples: valsartan, candesartan, losartan
- Should not be considered equivalent or superior to ACE inhibitors
- In clinical practice, ARBs should be used to treat patients who are ACE intolerant due to intractable cough or who develop angioedema

ARB's VS ACE-I

- Demonstrated similar effects as ACE
- ELITE II study: Losartan vs Captopril
- RESOLVD: Candesartan vs Enalapril
- No difference in outcomes
- Recommended if ACE not tolerated
- Combined ACE & ARB?
  - CHARM Added and Val-HeFT- benefit of ACE and ARB if not on B-Blocker, no difference or worse if ACE and B-Blocker
  - Good evidence for the use of ARBs to prevent events in patients on ACE not suitable for B-blockers

B-Blockers

- Cardioprotective effects due to blockade of excessive SNS stimulation
- In the short-term, beta blocker decreases myocardial contractility…but increase in EF after 1-3 months of use
- Improve functional class
- When combined with conventional HF therapy, beta-blockers reduce the combined risk of morbidity and mortality 30-60%

1 Hunt, SA, et al ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult, 2001 p. 20.

B Blocker Trials in Heart Failure

Prospective Mortality Trials:

- **MERIT-HF**
  - **TOPROL-XL vs. placebo**
- **COPERNICUS**
  - **carvedilol vs. placebo**
- **US Carvedilol Program**
- **COMET- cardevedilol may be better**
- **Can you use generic?**

B-Blocker Tips

- **Bisoprolol: starting dose 2.5-5mg once daily orally; target dose 10mg once daily**
- **Carvedilol: starting dose 3.125mg twice daily orally; target dose 25mg twice daily**
- **Metoprolol succinate: starting dose 12.5-25mg once daily orally; target dose 200mg once daily**
- **Lower ACE to allow B-Blocker**
- **Slow titration to highest dose tolerated**
- **Do not abruptly discontinue any beta-blocker – even if hospitalized**
- **Do not start in *decompensated* HF- diuretic and ACE first**
- **All patients with class II-III HF due to LV systolic dysfunction**
- **Class IV appears beneficial - COPERNICUS**

Aldosterone Antagonists- Spironalactone

- We used to think this was a benign player
- Causes salt/H2O retention, incr LV mass, wastes K and Mg- arrythmia, endothelial dysfx
- RALES Study
  - Spironolactone 25 mg po qd
  - Class III-IV HF with EF < 35%
  - 30% reduction in mortality
  - Use limited by side effects
- Generally well-tolerated
- SE include hyperkalemia and gynecomastia
- Closely monitor K+ and Cr levels

Diuretics

- Used to relieve fluid retention
- Improve exercise tolerance
- Facilitate the use of other drugs indicated for heart failure
- Patients can be taught to adjust their diuretic dose based on changes in body weight
- Electrolyte depletion a frequent complication
- *Should never be used alone to treat heart failure*
- Higher doses of diuretics are associated with increased mortality

Diuretics

- **Loop diuretics first line therapy**
  - **Furosemide: 20-40 mg po qd**
- **HCTZ added for refractory fluid overload if Cr Clearance > 35**
  - ***Increases potassium, magnesium wasting***
- **Metolazone 2.5 – 5.0 mg prior to loop (synergy) or Bumex 2-4 mg po qd in refractory fluid overload- *expensive***
- **Goals:**
  - **Adequate renal perfusion**
  - **No hypotension**
  - **Stable weight**
  - **Slight bump in creatinine expected**

Digoxin

- Enhances inotropy of cardiac muscle- CA+
- Reduces activation of SNS and RAAS
- Controlled trials - long-term digoxin therapy:
  - Reduces symptoms
  - Increases exercise tolerance
  - Improves hemodynamics
  - Decreases risk of HF progression
  - Reduces hospitalization for decompensated HF
  - low serum digoxin concentration (<0.09 ng per milliliter) is effective - 0.125 to 0.25 mg po qd
  - Control ventricular rate in AFIB
  - Does not improve survival
- Add to ACE-I, Diuretics, B-blockers in class II-IV HF

Other Inotropic Drugs

- Recent trials show an increase in mortality
- OPTIME HF- increase mortality with Milrinone and ischemic heart disease
- Used as a bridge to transplant
- Probably only indicated in the most severe cases of HF under the supervision of a HF specialist

Hydralazine and Isosorbide

- Combination decreases mortality in HF
- Enalapril had larger mortality benefit when directly compared (18% vs 25%)
- Intolerable side effects at target doses
- Use if ACE-I not tolerated or if renal insufficiency

Nesiritide (Natrecor)

- Increases sodium excretion and promotes vasodilation
- Exerts beneficial hemodynamic effects in decompensated CHF
    - Decrease in PCWP, SVR, RA pressure
    - Increase in cardiac index
- Improved dyspnea score, incr UOP
- But… higher mortality than NTG (VMAC trial)

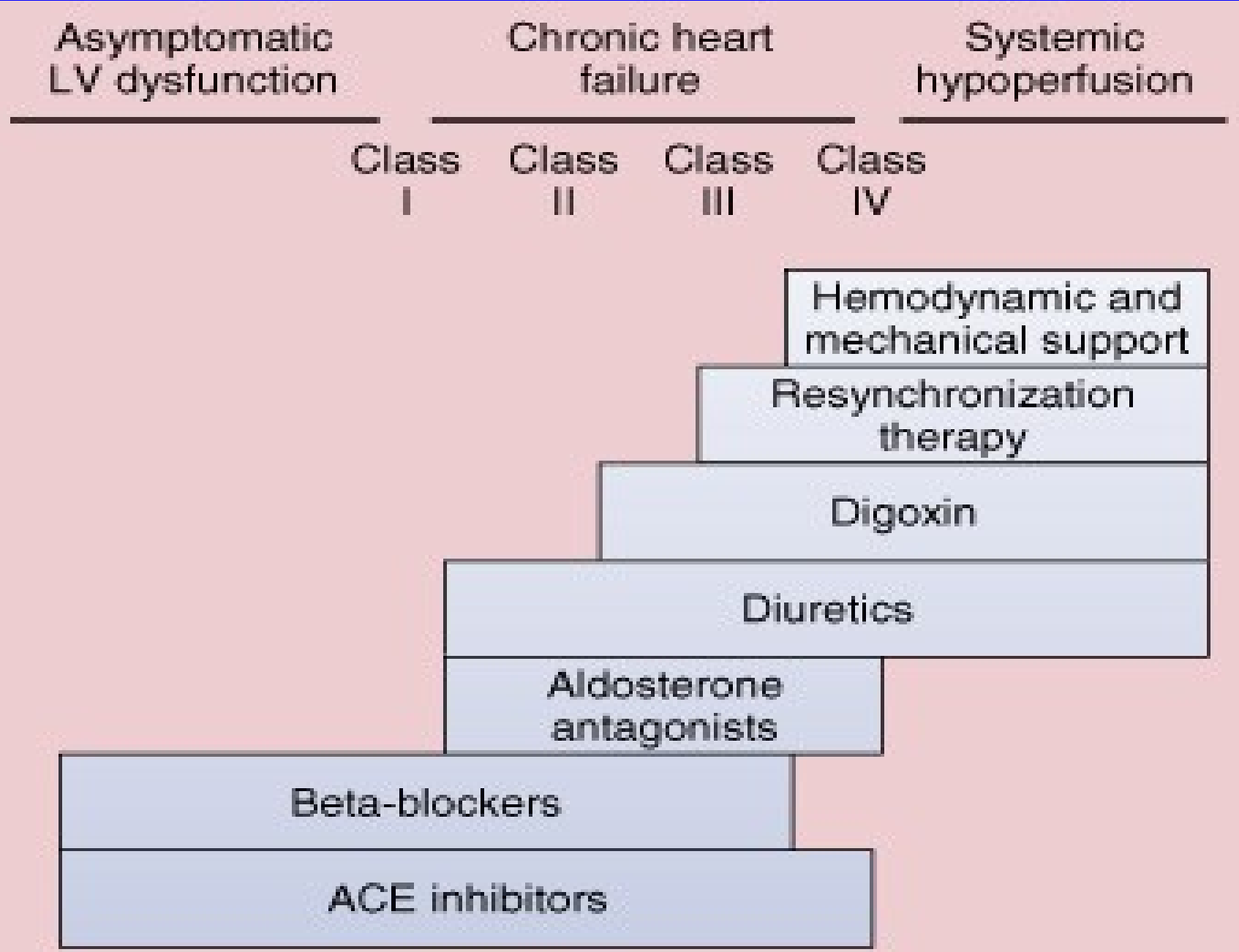
Anticoagulation

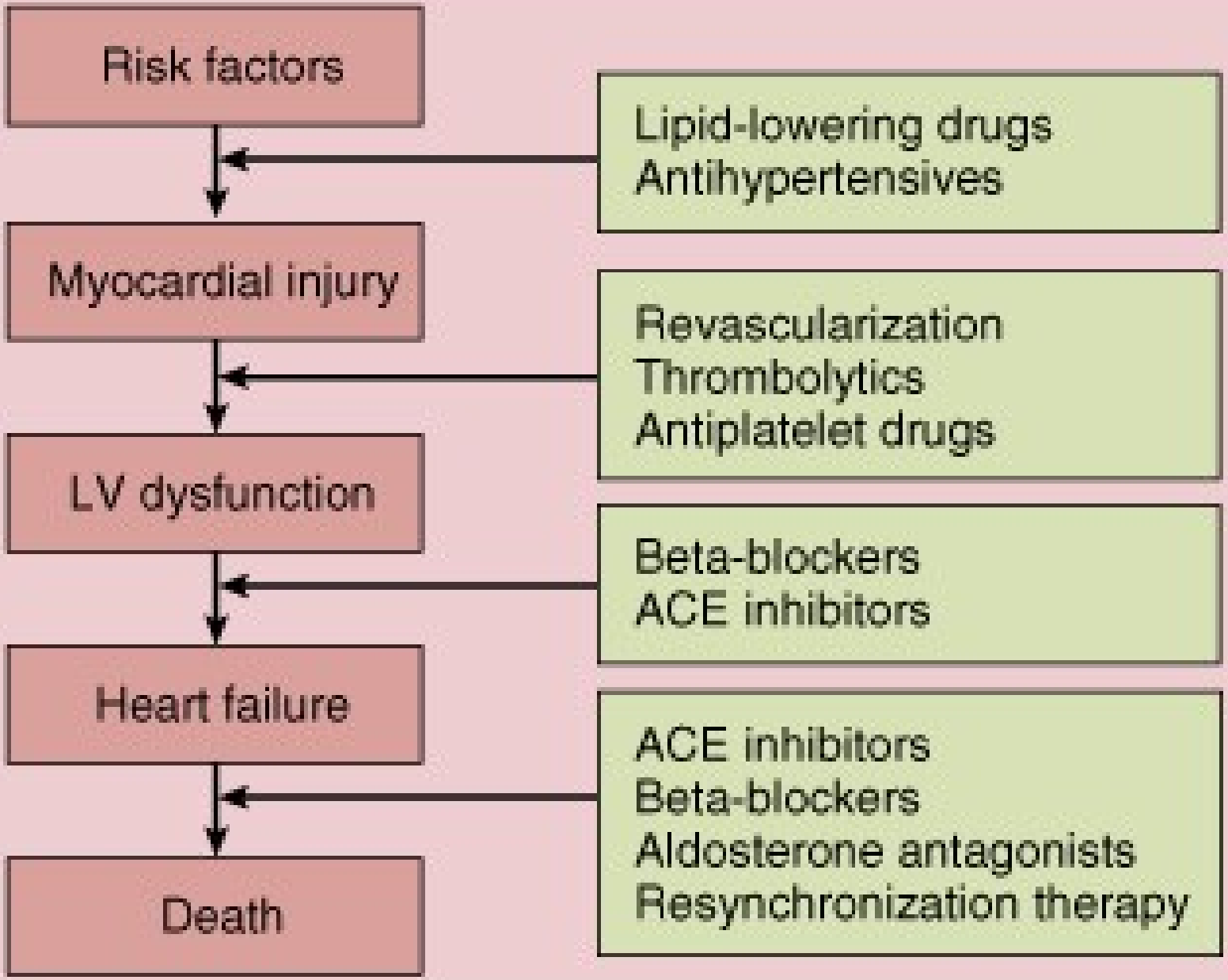
- Indicated in chronic A Fib or known thrombus
- Controversial in diminished LV Dysfunction without A Fib
- Current ongoing studies to assess:
  - WATCH and WARCEF combined will have enough power to determine if stroke risk reduced when EF< 30%

Drugs to Avoid in Heart Failure

- NSAIDS, incl COX 2
  - Incr edema, exacerbate CHF
- Calcium Channel Blockers
  - Worsen symptoms of HF, esp systolic dysfx
- Metformin
  - Risk of lactic acidosis in renal failure
- TZDs
  - Incr edema
- Antiarrythmics
  - Incr sudden death

Palliative Care for Patients With Heart Failure JAMA **Vol. 291 No. 20, M**





Cardiac Resynchronization Therapy

Patient Indications

CRT device:

- **Moderate to severe HF (NYHA Class III/IV) patients**
- **Symptomatic despite optimal, medical therapy**
- **QRS $\geq$ 130 msec**
- **LVEF $\leq$ 35%**

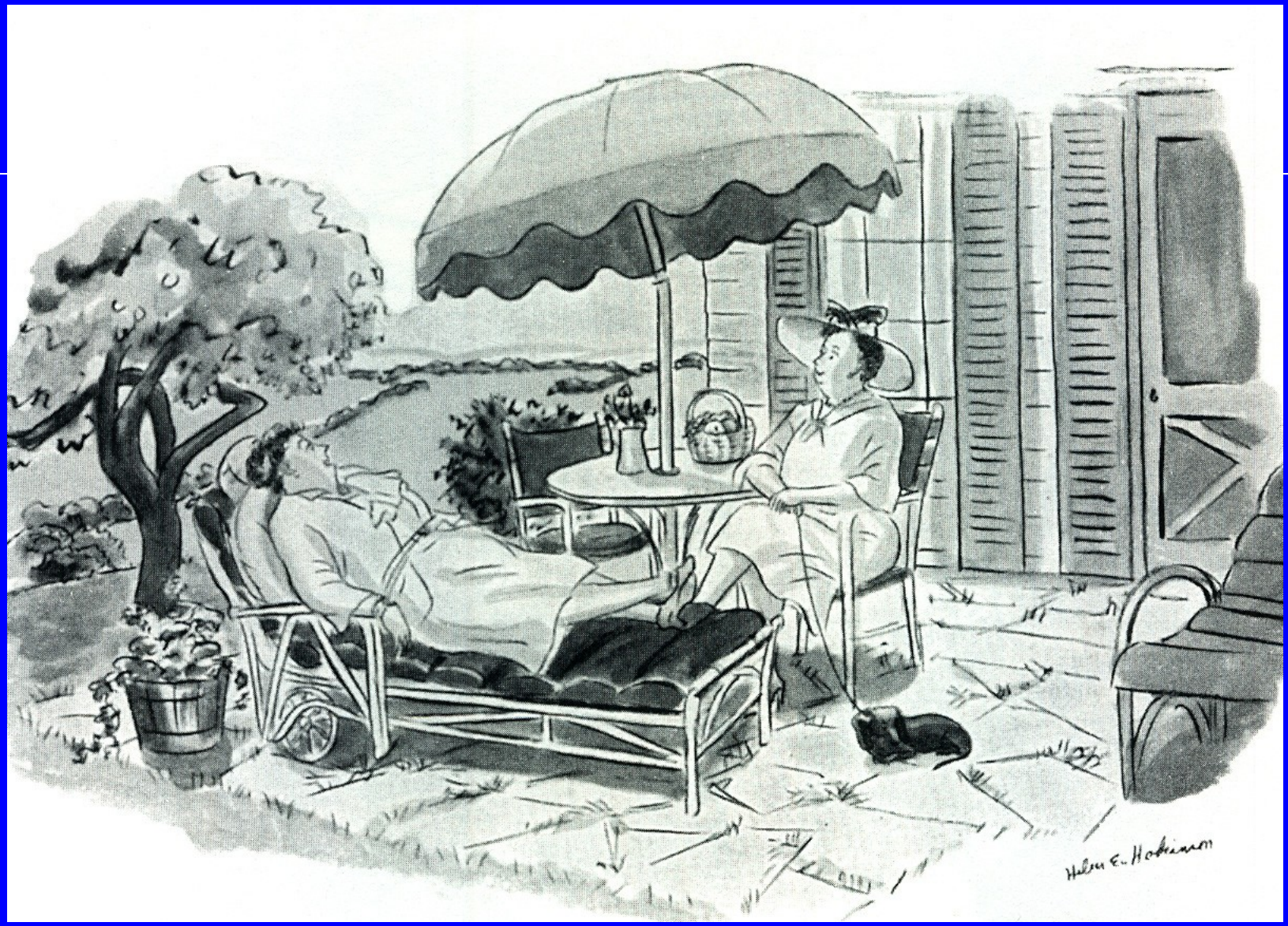
CRT plus ICD:

- **Same as above with ICD indication**

Emerging Therapies-Cardiac Resynchronization

COMPANION Trial- NEJM May 20, 2004

- Tested cardiac-resynchronization therapy in patients with CHF and intraventricular conduction delays
- Combined end point of death from or hospitalization for heart failure was reduced by 34 percent in the pacemaker group and by 40 percent in the pacemaker–defibrillator group
- A pacemaker reduced the risk of the secondary end point of death from any cause by 24 percent and a pacemaker–defibrillator reduced the risk by 36 percent
- **Concl: In patients with advanced heart failure and a prolonged QRS interval, cardiac-resynchronization therapy decreases the combined risk of death from any cause or first hospitalization and, when combined with an implantable defibrillator, significantly reduces mortality.**



You’d love my doctor. His creed is rest, rest, and more rest.

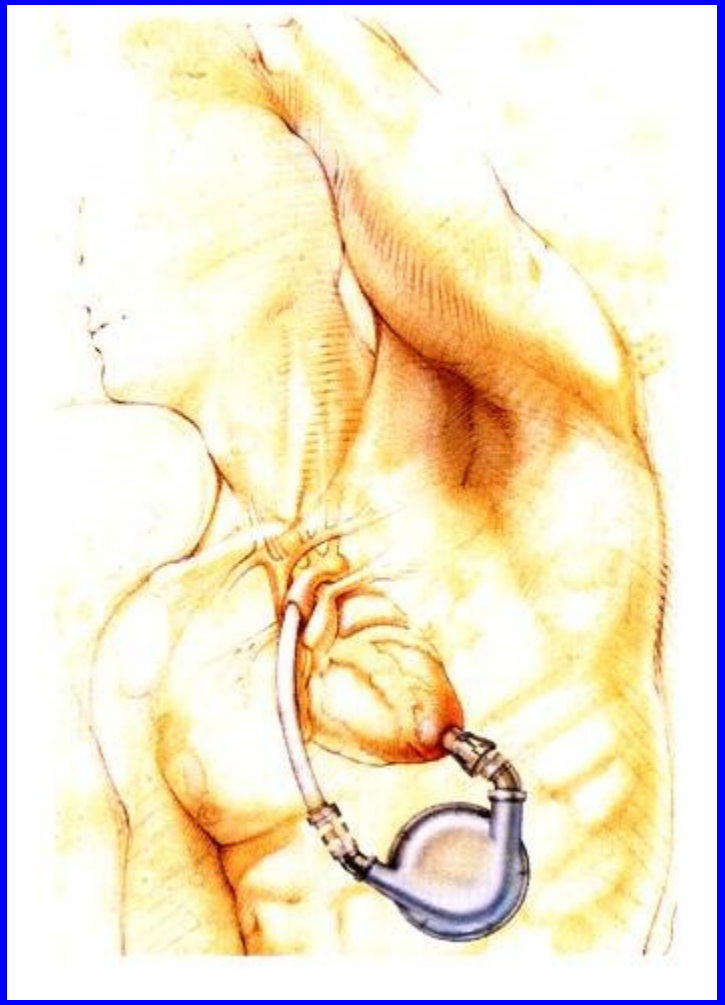
Exercise

ExTraMATCH Collaborative. *BMJ USA* 2004;4:109-112.

- In the not-too-distant past, clinicians were apprehensive about exercise for patients with chronic heart failure (CHF)
- Meta-analysis data from 9 studies (n = 801)
- Exercise programs attained peak oxygen consumption intensity ranging from 50-80%, by means of cycling, walking, or other aerobic activities
- All programs provided supervised activity, ranging from 30-60 minutes per day on multiple days per week
- Followup was up to approximately 2 years
- No changes in ACE inhibitors, beta blockers, or antialdosterone agents occurred during exercise study periods
- Exercise provided a favorable 35% risk reduction in mortality and 28% reduction in the combined end point of death or hospitalization

Other Surgical Therapy

- Cardiomyoplasty
- Ventriculectomy
- Heart Transplant
- Ventricular Assist Devices- REMATCH



Multidisciplinary Approach

- Lifestyle modification
  - Exercise, low Na+
- Case management
- Pharmacologic Interventions
- Treat underlying causes:
  - Treat CAD and Hypertension
  - Prevention decreases risk of HF
    - SHEP trial ↓ 81%
    - 4S trial ↓ 20%
    - HOPE trail

Treatment Approach for the Patient with Heart Failure

Stage A	Stage B	Stage C	Stage D
At high risk, no structural disease	Structural heart disease, asymptomatic	Structural heart disease with prior/current symptoms of HF	Refractory HF requiring specialized interventions
Therapy • Treat Hypertension • Treat lipid disorders • Encourage regular exercise • Discourage alcohol intake • ACE inhibition	**Therapy** • All measures under stage A • ACE inhibitors in appropriate patients • Beta-blockers in appropriate patients	**Therapy** • All measures under stage A Drugs: • Diuretics • ACE inhibitors • Beta-blockers • Digitalis • Dietary salt restriction	**Therapy** • All measures under stages A,B, and C • Mechanical assist devices • Heart transplantation • Continuous (not intermittent) IV inotropic infusions for palliation • Hospice care

Hunt, SA, et al ACC/AHA Guidelines CHF, 2001

Palliative Care for Patients With Heart Failure JAMA Vol. 291 No. 20, May 26, 2004

- Give prognosis
- Involve family
- Advanced directives and personal treatment goals
- Treat dyspnea
  - Oxygen, opiates
- Treat Pain
  - Opiates, NOT NSAIDS
- Treat depression
- Address fatigue
- Hospice and concurrent care programs

Unresolved Issues and Future Questions

- Anticoagulant therapy in severe heart failure?
- Optimal care for patients with heart failure and preserved systolic function (diastolic heart failure)?
- Revascularization in HF patients without angina?
- Identifying familial cardiomyopathy at an earlier stage?
- How do we identify patients with the greatest risk of sudden death?
- Best way to prevent sudden death in a cost-effective manner?
- Who will be best served by mechanical cardiac-support devices? AICD's?
- Can we afford optimal care for the growing number of heart failure patients?
- ***Most intensive efforts for prevention?***
  The control of hypertension and vascular risk factors